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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,323	08/01/2005	Christopher Robin Lowe	GJE-7169	5107
23557 7590 01/17/2008 SALIWANCHIK LLOYD & SALIWANCHIK A PROFESSIONAL ASSOCIATION PO BOX 142950 GAINESVILLE, FL 32614-2950			EXAMINER SCHUBERG, LAURA J	
			ART UNIT 1657	PAPER NUMBER
			MAIL DATE 01/17/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/520,323

Applicant(s)

LOWE ET AL.

Examiner

Laura Schuberg

Art Unit

1657

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 23-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☒ Claim(s) 19 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>4/11/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I (claims 1-22) in the reply filed on 11/05/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-35 are pending.

Claims 23-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-22 have been examined on the merits.

Claim Objections

Claim 19 is objected to because of the following informalities: the claim recites the limitation "introducing a component of or derived from the cells". This wording is not grammatically correct. Commas inserted before "or" and after "derived from", would improve the clarity of the claim (introducing

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-22 are rejected under 35 U.S.C. 101 because the subject matter claimed by independent claim 1 does not fall into a single statutory class of invention, as it claims both a method and a device, therefore it is directed to neither a method or a device, but rather encompasses or overlaps two different statutory classes of invention. The language of 35 USC 101 prohibits overlap between two different statutory classes in a single claim as it is drafted so as to set forth the statutory classes of invention in the alternative only. See *Ex parte Lyell*, 17 USPQ2d 1551 (Bd. Pat. App. & Inter. 1990).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's claims 1-22 are ambiguous, and thus indefinite, because they are directed to both a method and a device; therefore it is not clear what applicant is intended to claim: a method or a device. See *Ex parte Lyell*, 17 USPQ2d 1548 (Bd. Pat. App. & Inter. 1990) & MPEP 2173.05(p). While the claim is indefinite, in order to provide

compact prosecution, the claims will be examined as method claims (a method of using the device).

In addition, while the claims are drawn to method for monitoring cells, the claims do not contain any actual steps performing this method and as such are missing essential elements as well.

Claim 3 recites the limitation "the gas" in line 1. There is insufficient antecedent basis for this limitation in the claim. Since claims 1 and 2 do not recite any steps that include a gas, it is unclear which gas claim 3 is referring to. For examination purposes, the claim is interpreted as including the contacting of gas with the device.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 7-11, 13-16, 19-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Jensen et al (US 2004/0077075).

Claim 1 is drawn to a method for monitoring cells in a microfluidic device, wherein the device includes a chamber comprising a sensor, and the monitoring is under conditions such that attachment of cells to the surface of the chamber is inhibited.

Dependent claims include wherein the chamber surface comprises a gas-permeable material (claim 2); wherein the gas is selected from a group (claim 3); wherein the material is a fluoropolymers (claim 4); wherein the chamber surface comprises a hydrophilic material (claim 5); wherein the chamber is formed in epoxy resin coated on a plastics substrate (claim 7); wherein the plastics substrate is polycarbonate (claim 8); wherein the chamber comprises a plurality of sensors (claim 9); wherein the sensor is sensitive to oxygen, carbon dioxide, ammonium or pH (claim 10); wherein the sensor is optical or electrochemical or acoustic (claims 11 and 13); wherein the sensor is sensitive to a reactant or product of fermentation (claim 14); wherein the volume of the chamber is from 50 nL to 10 μ L (claim 15); further comprising introducing growth medium into the chamber, wherein the sensor is sensitive to a reactant or product of cell growth (claim 16); further comprising introducing a component derived from the cells into a second microfluidic chamber comprising a sensor and in connection with the first chamber detecting the component (claim 19); wherein the component is a product of cell growth (claim 20); wherein the component is an expressed protein or enzyme (claim 21) and wherein the sensor of the second chamber is as defined in any of claims 10-15 (claim 22).

Jensen et al teach a microfluidic device for use in monitoring and culturing cells. The microfluidic device is a vessel having an interior volume of less than 200 ml and

in particular 5 ml (page 3 para50) and which has an aeration membrane made of a fluoropolymer or silicone that allows oxygen diffusion to the growing cells (page 8 para 94). The surface of the chamber is modified to inhibit attachment of cells (page 8 para 97-99) and at least one analytical sensor is integrated into the device (page 10 para 112). Wherein the chamber surface comprises a hydrophilic material is taught (page 8 para 98-99) as well as wherein the chamber comprises a plurality of sensors, including optical and electrochemical (page 11 para 116) that are sensitive to oxygen, carbon dioxide or pH (page 11 para 117-127). The chamber is formed in an epoxy resin coated on a plastics substrate (page 18 para 206) and the substrate material includes polycarbonate (page 4 para 62). The analytical sensor detects or measures (is sensitive to) any cell metabolite or cell product such as a protein or enzyme (page 10 para 112). Introducing growth medium into the chamber, wherein the sensor is sensitive to a product of cell growth, is taught (page 1 para 7) as well as introducing a component derived from the cells into a second microfluidic chamber comprising a sensor and connected by a membrane with the first chamber detecting the component (page 1 para 10).

Therefore, the teaching of Jensen et al anticipates Applicant's invention as claimed.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jensen et al (US 2004/0077075) as applied to claims 1-5, 7-11, 13-16, 19-22 above, and further in view of Wada et al (WO 99/67639-from IDS).

Claim 6 is drawn to the method of claim 5 and includes wherein the hydrophilic material is polyvinyl alcohol.

Jensen et al teach the method of using the microfluidic device as described above and indicate that a number of different approaches may be employed to alter the adsorptive properties of the contacting surfaces of the device and provide a hydrophilic surface (page 8 para 98-99).

Jensen et al do not specifically teach the use of polyvinyl alcohol as a hydrophilic material.

Wada et al teach a method for monitoring cells with a microfluidic device. The prevention of attachment of the cells to the interior surface of the device is taught as desirable and accomplished in a variety of ways such as using PVA (polyvinylalcohol) coatings (page 25 line 31-page 26 line 7).

Therefore, one of ordinary skill in the art would have been motivated to use PVA as a coating on the surface of the microfluidic device of Jensen et al because Wada et al teach that a PVA coating is a suitable treatment to prevent cell attachment in a microfluidic device and Jensen et al teach the desire to prevent cell attachment as well. One of ordinary skill in the art would have had a reasonable expectation of success because both Jensen et al (page 8 para 95) and Wada et al (page 24 line 18) are using microfluidic devices of the same material (PDMS).

Therefore, the combined teachings of Jensen et al and Wada et al render obvious Applicant's invention as claimed.

Claim 12 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jensen et al (US 2004/0077075) as applied to claims 1-5, 7-11, 13-16, 19-22 above, and further in view of Lowe et al (US 5,989,923).

Claim 12 is drawn to the method of claim 11, wherein the sensor is a holographic sensor.

Jensen et al teach the method of using the microfluidic device as described above and indicate that there is a need to integrate available sensor technology (page 3 para 49).

Jensen et al do not specifically teach the use of holographic sensors with the microfluidic device.

Lowe et al teach a holographic sensor for measuring analytes (column 11 lines 18-46). In particular the sensor has applications in detecting biologically secreted proteins or proteases and is capable of detecting bacteria.

Therefore, one of ordinary skill in the art would have been motivated to apply the holographic sensors of Lowe et al to the microfluidic device of Jensen et al because Jensen et al indicate that more than one type of optical sensor may be used in the device to monitor cells (such as bacteria) and because Lowe et al teach that holographic sensors are suitable for optically interrogating bacteria. One of ordinary skill in the art would have had a reasonable expectation of success because Lowe et al teach that it is readily apparent that a holographic sensor may be fabricated whose characteristics are predictable (column 11 lines 22-25).

Therefore, the combined teachings of Jensen et al and Lowe et al render obvious Applicant's invention as claimed.

Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jensen et al (US 2004/0077075) as applied to claims 1-5, 7-11, 13-16, 19-22

above, and further in view of Walker et al (US 5,474,774) and Qian et al (Analytical Chemistry 2002).

Claim 17 includes wherein the growth medium comprises a non-metabolisable mannose analogue.

Claim 18 includes wherein the analogue is methyl α -D-mannopyranoside.

Jensen et al teach the method of using the microfluidic device as described above and indicate that different approaches may be employed in inhibiting the attachment of the cells (pages 9-10, para 107).

Jensen et al do not specifically teach the addition of a non-metabolisable analogue of mannose, such as methyl α -D-mannopyranoside.

Walker et al teach a method of inhibiting the adhesion of bacteria to devices, such as fermentation equipment, by applying an extract to a suitable medium to a surface having bacteria to disengage the bacteria from the surface (column 2 lines 32-49).

Qian et al teach that methyl α -D-mannopyranoside is a compound that inhibits the adhesion of bacteria to surfaces (page 1808, column 2).

Therefore, one of ordinary skill in the art would have been motivated to use the non-metabolisable analogue of methyl α -D-mannopyranoside as a compound to prevent bacterial adhesion in the device of Jensen et al because Walker et al teach that it is known in the art to add compounds that inhibit bacterial adhesion to a surface, such as a fermentation device, in a suitable medium and Qian et al teach that methyl α -D-mannopyranoside is capable of inhibiting bacterial adhesion. One of ordinary skill in the

art would have had a reasonable expectation of success because Jensen et al indicate that different approaches may be employed in inhibiting the attachment of the cells (pages 9-10, para 107).

Therefore, the combined teachings of Jensen et al., Walker et al and Qian et al render obvious Applicant's invention as claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 9-12, 14, 16, 19, 20, are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7, 8, and 14 of copending Application No. 10/520331. Although the conflicting claims are

not identical, they are not patentably distinct from each other because they disclose inventions with the same limitations. It is noted that instant claim 1 requires that the cell is inhibited from attachment to the surface of the chamber, whereas claim 1 of copending 10/520221 requires that the cell be immobilized. However these limitations do not exclude wherein a cell is immobilized on a bead that is then inhibited from attachment to the surface of the chamber. Therefore the claims, as recited, are overlapping.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

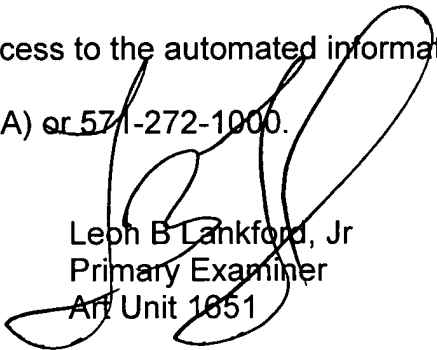
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura Schuberg whose telephone number is 571-272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Leon B Lankford, Jr
Primary Examiner
Art Unit 1651

Laura Schuberg